

### **Remarks/Arguments**

Claims 1 to 22 are pending. Claims 1, 5, 6, 10, 12, 13, 17 and 19 to 22 have been amended. Claims 2 to 4, 11 and 18 have been cancelled.

Applicants have amended the claims to recite only tetrahydrofuran. Water-miscible organic solvent A has been limited to tetrahydrofuran. Water-miscible organic solvent B has been limited to tetrahydrofuran. Support for these amendments is found on page 4, lines 23 to 31. Tetrahydrofuran is stated to be most preferable of the water-miscible organic solvents. Note also that tetrahydrofuran is used as both water-miscible organic solvents A and B in Example 2. Also the recrystallization in Claims 10 and 17 has been limited to using a mixture of methanol and tetrahydrofuran. Further note that Example 3 uses a mixture of methanol and tetrahydrofuran.

Claims 1 to 22 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Omura et al. (U.S. Patent No. 4,107,297; cited in the IDS filed January 4, 2008) in view of Hershberger et al. (U.S. Patent No. 4, 637,981), Borghi et al. et al. (U.S. Patent No. 5,135,857) and Nabais (1995). Applicants traverse this rejection.

Applicants' claims use the filtration method. Staurosporine is insoluble in water (Omura et al., col. 2, lines 8 and 9). Before the ultrafiltration step, applicants add tetrahydrofuran to the fermentation broth. Tetrahydrofuran is very soluble in water. Staurosporine is soluble in tetrahydrofuran. The ultrafiltration step separates microbial bodies in the fermentation broth and the filtrate which contains the staurosporine in the mixture of water and tetrahydrofuran. (Applicants' method then goes on to concentrate the filtrate, adjusting the pH to at least 8.5 {if not already at that pH}, and collecting the precipitated staurosporine.)

While Omura et al. mentions the filtration separation method, Omura et al. does not give any specifics of such process. Omura et al. does not mention tetrahydrofuran as a suitable solvent for any separation method (let alone the filtration separation method) for the recovery of staurosporine from fermentation broth.

Instead, Omura et al. concentrates on the entirely different solvent extraction method (with no mention of using tetrahydrofuran). A review of the portions of Omura et al. on the solvent extraction method does not show the use of a filtration separation step therein.

One ordinarily skilled in the art is not going to combine Hersberger et al. with Omura et al. in the quest for applicants' claimed invention. The two patents are directed at solving different problems. Omura et al. is seeking to recover a water insoluble chemical entity from a fermentation broth, whereas Hersberger et al. is seeking to recover a water soluble chemical entity from a fermentation broth. There has been no showing of record why one ordinarily skilled in the art trying to recover one of the two types of chemical entities would look to a patent/reference dealing with the other type of chemical entity. Along the same lines, the antibiotic entity sought by Hersberger et al. is not soluble (i.e., insoluble) in solvents such as methanol, acetone, diethyl ether, chloroform, benzene and the like, whereas Omura et al. states that that which it seeks is soluble (or at least sparingly soluble) in methanol, chloroform, ethyl acetate, n-butyl acetate, dimethyl sulfoxide and dimethyl formamide.

Column 9, lines 29 to 58, and the examples of Hersberger et al. involves use of the filtration separation method to separate out its water insoluble chemical entity (followed by further steps). Hersberger et al. is not pertinent to the problem of recovering water soluble staurosporine. Hersberger et al. apparently does not anywhere mention tetrahydrofuran.

The pH of the steps in Hersberger et al. following filtration is never as high as that recited in applicants' recovery step. The pH of at least 8.5 is required by applicants to effectively precipitate the staurosporine – the lower pH of Hersberger et al. would not result in any meaningful precipitation of staurosporine required by applicants' claimed process.

The other two secondary rejection references in the rejection combination do not cure the defects of Omura et al. and Hersberger et al. (separately or together) in the quest for applicants' claimed invention. Borghi et al. discloses using tetrahydrofuran in affinity

chromatography directly after filtration or a preliminary purification procedure – this has nothing to do with applicants' claimed process. Borghi et al. also does not deal with staurosporine.

Tetrahydrofuran is advantageous over, for example, acetone or simple alcohols (C<sub>1-3</sub>) since acetone and simple alcohols dissolve too little staurosporine and, thus, would have to be used in very large quantities. Hershberger et al suggests the use of acetone for the purification its water soluble antibiotic.

The bio-broth from *Streptomyces* fermentation is highly viscous. Dilution with water soluble organic solvent, especially tetrahydrofuran, reduces the viscosity and thereby increases the permeate flow considerably, rendering the the ultrafiltration process more attractive. Hershberger et al. uses filtration but not disclose that it is ultrafiltration.

Tetrahydrofuran is preferred over an extraction separation method since, in view of the low solubility of staurosporine, a large volume of solvents would be required and, furthermore, other components such as sugar derivatives would be co-extracted which later disturb the crystallization process.

The limitation of the claims to tetrahydrofuran is believed to make them allowable and patentable even over the rejection combination.

The Office Action stated that applicants argued that the Examiner has incorrectly attempted to generify the limited disclosure of Omura et al. and that Omura et al. does not disclose the recovery of staurosporine from a fermentation broth. Applicants' assertion is not argument but instead is factual.

The Office Action stated that applicants argued that Omura et al. teaches away from diafiltration because Omura et al. discloses that staurosporine is fat soluble and that the loss of product from ethyl acetate results in the loss of some staurosporine. Applicants' assertion is correct.

The Office Action stated that applicants asserted that "Omura et al. would teach extraction of AM-2282 with sparingly soluble in butyl acetate and one of ordinarily skilled in the

art would be directed away from the use of Omura et al. in the search for the claimed invention.” Applicants’ assertion is correct and the Examiner has not proven otherwise.

The Office Action stated that applicants argued that Omura et al. extracts AM-2282 from water using ethyl acetate, which directs away from applicants’ use of a mixture of water and ethyl acetate (or other organic solvent B)) to extract from the retentate of the diafiltration, thus showing the unobviousness of Claims 6, 11 to 13 and 18. Applicants’ assertion is correct. Since applicants have limited their claims to organic solvent A and organic solvent B being tetrahydrofuran, Omura et al. even further directs away from applicants’ claimed invention.

The Office Action stated that applicants argued that the disclosure by Omura et al. of evaporation, chromatography on silica gel and recrystallization does not make instant Claim 10 obvious as a whole. Applicants’ assertion is correct because Section 103(a) requires consideration of applicants’ claimed as a whole, not as separate pieces.

The Office Action stated that applicants asserted that the statement by Omura et al. that staurosporine recovery can be achieved by “known methods for separating antibiotics” is so broad as to be meaningless under Section 103(a) and clearly would cover many of such process that would be inoperable for AM-2282 and applicants’ claimed process. Applicants’ assertion is correct and controlling, and the Examiner has not proven otherwise.

The Office Action stated that applicants argued that the rejection of Claims 2 to 11, 13 14 and 18, because they limit steps that are indicated as optional in Claim 1, has no basis in law and that the Examiner has not cited any support in law for his position. The position asserted by applicants is correct.

The Office Action stated that applicants concluded that said claims are allowable. Applicants’ position is correct.

The Office Action stated that applicants asserted that the term “optionally” means that there are two processes – one without the optional step included and one with the optional step included. The Examiner has not proven that applicants’ assertion is incorrect.

The Office Action stated that applicants cited M.P.E.P., 2173.05(h)(111), which states "...was considered acceptable alternative language because there was no ambiguity as to which alternatives were covered by the claim." The Examiner has not proven that the MPEP quotation is incorrect,

The Office Action stated that applicants asserted that the Examiner has not shown that any such ambiguity is present. Applicants' assertion is correct. The Examiner has the burden of proof under this Section 103(a) rejection to show factually in the record that such ambiguity is present (which the Examiner has not done), and the Examiner has not carried his burden of proof.

The Office Action stated that applicants asserted that the statement regarding what Omura et al. does not teach is an admission of nonobviousness.

The Office Action stated that applicants argued that the Examiner has not shown why one ordinarily skilled in the art would combine the three secondary rejection references with Omura et al. in the search for applicants' claimed invention. Applicants' assertion is correct. The Examiner has the burden of proof under this Section 103(a) rejection to show factually why one ordinarily skilled in the art would combine the three secondary rejection references with Omura et al. in the quest for applicants' claimed invention (note that the Examiner has not made such a factual showing in the record. The Examiner still has the burden of proof. Also, since the Examiner has not factually resolved, and shown factual support in the record for such resolution, the level of ordinary skill in the record, the Examiner has no basis for combining the four rejection references in this Section 103(a) rejection.

The Office Action stated that applicants argued that Hershberger et al. directs one ordinarily skilled in the art away from applicants' claimed invention because Hershberger et al. does not teach a basic pH which is required by the instant application. Applicants' assertion is correct.

The Office Action stated that applicants asserted that all of the teachings of a reference and the prior art of record must be considered under Section 103(a) and that when the teachings of the rejection references are in direct conflict and there is no basis for choosing one conflicting teaching over the other, there is no basis for a holding of obviousness. Applicants' assertions are correct in the patent law.

The Office Action stated that applicants argued that filtration with diatomaceous earth or other commercially available filter aids does not make the claimed invention obvious. The Examiner has not proven otherwise....

The Office Action stated that applicants argued that Hershberger et al. teaches centrifugation, evaporation and Hershberger et al.'s teaching that factor G can be isolated by conventional isolation features do not make the invention obvious. Hershberger makes applicants' claimed invention unobvious.

The Office Action stated that applicants argued that the Examiner has not demonstrated why the ordinary artisan would combine Hershberger et al. with the other references. Applicants' assertion is correct and the Examiner has not proven otherwise. Furthermore, the so-called ordinary artisan has nothing to do with Section 103(a); instead, it is one ordinarily skilled in the art that counts under Section 103(a).

The Office Action stated that applicants argued that the disclosure by Nabais and Borghi et al. make broad statements that do not make applicants' invention as a whole obvious. Applicants' assertion is correct (for example, an invention must be considered as a whole) and the Examiner has not proven otherwise. The Examiner's piece-meal approach is incorrect.

The Office Action stated that applicants argued that the assertion that Borghi et al. establishes that methods for the recovery of antibiotics from biological sources are well established in the art is broad statement that is meaningless. In the search for applicants' claimed invention the noted broad, generic statements of Borghi et al. carry little or no weight in the search for applicants' claimed invention under Section 103(a).

The Office Action stated that applicants argued that the Examiner had not determined in the record the level of ordinary skill in the art, without which a valid obviousness rejection can not be made. Applicants are correct; the Patent Office policy on the matter is controlling and shows that applicants are correct; and the involved Supreme Court decisions also show that applicants' position is correct.

The Office Action stated that applicants argued that the Examiner's use of the term "ordinary artisan" is meaningless under Section 103(a) because it is not the same as "the artisan ordinarily skilled in the art" ("one ordinarily skilled in the art") which is the standard required under Section 103(a). Applicants' assertion is correct in law and patent practice.

The Office Action stated that wherever the Examiner has used such term, the statement is meaningless under Section 103(a). Applicants' assertion is correct.

The Office Action stated that applicants argued that the citation of Ex parte Kubin, 83 USPQ2d 1410 (Bd. Pat. App. & Int., 2007), is not relevant because it only deals with the situation where the level of ordinary skill in the art has already been determined. The Examiner has not shown that the Board decision deals with a situation as in the present case.

The Office Action stated that applicants argued that the cited Board decision is not relevant to this case because it does not deal with the determination of the level of ordinary skill in the art but only deals with one ordinarily skilled in the art. The Examiner has not correctly set out applicants' position. The Board decision is not relevant because the level of ordinary skill in the art had already been determined.

The Office Action stated that applicants asserted that the Patent Office and Supreme Court requires determination of the level of ordinary skill in the art as a mandatory prerequisite before a valid decision of obviousness can be made under Section 103(a). There can be no dissent from or disagreement with such mandatory prerequisite by the Examiner because full and complete compliance by the Examiner with such prerequisite is required by Patent Office

policy (which comes from the Secretary Of Commerce and the Director Of Patents And Trademarks).

The Office Action stated that applicants asserted that all statements regarding the references, the combination of references and what a reasonable expectation is are meaningless under Section 103(a) because it is based upon “the ordinary artisan” and the Examiner does not know what would be a reasonable expectation to one ordinarily skilled in the art. Applicants’ position is correct – the Examiner has not determined the level of ordinary skill in the art so the Examiner cannot know anything about one ordinarily skilled in the art.

The Office Action stated that applicants argued that the claimed invention which teaches the addition of a water-miscible organic solvent such as methanol, ethanol, propanol, 2-propanol, tert-butanol, acetone or tetrahydrofuran and the adjustment to a pH of at least 8.5 in a method to purify staurosporine – is not obvious in view of the “(attempted) combination of references” cited by the Examiner. Applicants have shown that the use of tetrahydrofuran in applicants’ claimed process is not obvious over the rejection combination, The Examiner has not proven otherwise.

The Office Action stated that Omura et al. teaches the use of n-butyl acetate which is only slightly soluble in water (0.7% at 20 °C) and not the use of water-miscible organic solvent. This shows the unobviousness of applicants’ claimed process that now only claims tetrahydrofuran, that is very water soluble. Omura et al.’s use of the only-slightly-soluble-in-water n-butyl acetate directs away from applicants’ use very-soluble-in-water tetrahydrofuran.

The Office Action stated “[a]lthough Omura et al. states that staurosporine is only sparingly soluble in butyl acetate, there is no suggestion or motivation by Omura et al. to search for an alternative way of extracting staurosporine.” There is no basis for using Omura et al in the rejection combination in view of the claim amendments.

The Office Action stated: that “[f]urther, even though Hershberger et al. teaches the use of a water miscible organic solvent such as acetone for the isolation of an antibiotic, it should be



noted that staurosporine and factor G, i.e., the antibiotic of Hershberger et al., are different molecules having different solubility in different solvents.”; that applicants questioned whether a method which functions to isolate one antibiotic is also applicable for the isolation of a different antibiotic; that applicants pointed out that Hershberger et al. does not describe the use of a water miscible organic solvent alone, but instead teaches a combination of using a water miscible organic solvent such as acetone and subsequently the acidification of the whole diluted fermentation broth; that applicants concluded that Hershberger et al. teaches away from the instantly claimed invention which claims adjustment to a pH of at least 8.5; that applicants asserted that a multi-step process for the isolation of staurosporine is claimed and that a prior art document which describes only one step of such multi-step process does not make the claimed invention multi-step process obvious to one ordinarily skilled in the art; and that applicants argued that the attempted combination of rejection references directs away from applicants’ claimed invention. Applicants’ assertion are correct, particularly in regard to the amended claims.

Applicants point out that the Examiner’s recitation of applicants’ arguments, assertions, conclusions, etc., is incorrect in many places.

The Office Action stated: that in response to applicants’ argument regarding the generification of Omura et al., that Omura et al. does not teach the isolation of staurosporine from a fermentation broth, the claims and specification (see the examples) in the Omura et al. patent are drawn to the fermentation and recovery of staurosporine; that this representation by the Examiner’s of applicants’ arguments is seriously in error; that, responding to applicants’ assertion that Omura et al. teaches away from diafiltration due to loss of product, a 100% recovery of product from any purification is extremely rare and it is unclear why an expected loss of product during isolation teaches away from diafiltration; that, previously, the rejected claims did not recited a diafiltration step due to the alternative language (“optionally”) the diafiltration steps was not considered since one has the choice of executing the step; that the

claims were rejected based on the alternative that the diafiltration step is not performed; that new Claims 19 to 22 require ultrafiltration and diafiltration; that Nabais disclose the ultrafiltration in combination with diafiltration of fermented broths containing antibiotics (note the generification for all antibiotics) using FP10 membrane is a valid alternative to the use of rotary vacuum filters, flocculants and filter aids (abstract); that, hence, the ordinary artisan would have been motivated to modify the combined disclosures of Omura et al., Hershberger et al. and Nabais and to employ ultrafiltration in combination with diafiltration to obtain staurosporine from a fermented broth because the method is superior to older methods of filtration of product; and that the ordinary artisan would have had a reasonable expectation of success because Nabais discloses the success for obtaining clavulanic acid using the combined method (see Table 6). This statement is full of errors as applicants have shown. Furthermore, this statement does not address the amended claims.

The Examiner keeps erroneously using the so-called ordinary artisan as the standard under Section 103(a). Note that the Supreme Court in its KSR decision used the standard “a person of ordinary skill” in the art, not “the ordinary artisan”. The Office Action is defective throughout because of this reason.

The Office Action stated: that regarding applicants’ assertion that staurosporine was sparingly soluble in butyl acetate and teaches away from the invention, Omura et al. specifically teaches that the extraction can be performed with an “suitable solvent” (col. 6, lines 55 to 57); that this is a clear indication that the ordinary artisan that Omura et al. expects that the ordinary artisan can select an extraction solvent; and that, furthermore, the ordinary artisan would have been motivated to employ a miscible solvent given the low solubility in water and butyl acetate. This statement has also been shown to be full of errors and does not treat the claims as amended.

The Office Action stated: that responding to applicants’ argument that Omura. et al’s. extraction of staurosporine with ethyl acetate teaches away from Claims 6, 11 to 13 and 18, the

claims were rejected because they limit steps that are indicated as optional in Claim 1; that, for the purposes of this rejection, the claims were interpreted that the optional steps are not performed; and that, responding to applicants' argument that Omura et al's disclosure of evaporation, etc., and the motivational statement that clearly teaches the purification of staurosporine can be purified by known methods do not make the instant claim obvious as a whole, the argument is non-persuasive because that are allegations without factual support. Applicants traverse this statement. The burden of proof is on the Examiner – it is the Examiner's burden to prove his statements and obviousness. Applicants have shown that this rejection is basically faulty in fact and law, and fails a priori.

The Office Action stated: that, responding to applicants' assertion that there is no basis in the law for not examining Claims 2 to 11, 13, 14 and 18, this argument is not persuasive because it is clear that the dependent claims can depend from the option of diafiltering, which is clearly indicated optional; that the dependent claims do not specifically marry the dependent limitations to one alternative (performing step iii) or not performing step (iii); that the Examiner concurs with applicants' meaning of "optionally" because it clearly defines "optionally" that there are two processes – one without the optional step included and one with the optional step included."; that, hence, "optionally" indicates that the optional steps are in the alternative (e.g., they are performed or they are not performed); and that the Examiner agrees that ambiguity has not been shown because the alternative language implied by "optional" is clear. The Examiner's position is in error because the independent claim is not obvious, hence the dependent claims cannot be obvious. The US does not use the old European system.

The Office Action stated: that applicants' assertion with respect to what Omura et al. does not teach or is not an admission of nonobviousness; and that it is a well known standard for the factual inquiries set forth in *Graham v John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The Examiner has not factually resolved the level of ordinary skill in the art, as should have been done in an earlier Office Action, so this Section 103(a) is fatally defective.

The Office Action stated that applicants' assertion that the Examiner has not demonstrated the motivation for the combination of references is, again, an allegation without factual support and, therefore, non-persuasive. Applicants' position is correct. This a legal matter. The Examiner has the burden of proof.

The Office Action stated that responding to applicants' arguments that Hershberger et al. does not teach a basic pH, that Hershberger et al.'s use of conventional isolation procedures and the Examiner has not demonstrated a motivation to combine Hershberger et al. with the other references, the arguments are non-persuasive because they are allegations without factual support (e.g., in what way has the Examiner failed to show a lack of motivation to combine references when such statements are made in the rejection?). The Examiner's position has been and challenged so it is the Examiner's burden prove his assertion is factually and legally supported and correct

The Office Action stated that responding to applicants' assertion that Nabais and Borghi et al. make broad statements do not make applicants' invention as a whole obvious, this argument is non-persuasive because it is an allegation without factual support, and therefore, non-persuasive. The Examiner has the burden to proof his position is correct because it has been challenged/traversed.

The Office Action stated: that responding to applicants' assertion that the term "ordinary artisan" is meaningless and not the same as the "artisan ordinarily skilled in the art," any

practitioner in the field of patents would recognize that the phrase “ordinary artisan” is a synonym for “artisan ordinarily skilled in the art”; and that applicants are directed, for example, directed to MPEP page 2100 to 2112 under Section C): “requires a determination of the level of skill of the ordinary artisan” or MPEP 2143, part g:

“The Courts have made clear that the teaching, suggestion, or motivation test is flexible and an explicit suggestion, or motivation test is flexible and an explicit suggestion to combine the prior art is not necessary. The motivation to combine may be implicit and may be found in the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. *Id.* At 1366, 80 USPQ2d at 1649. “[A]n implicit motivation to combine exists not only when a suggestion may be gleaned from the prior art as whole, but when the ‘improvement’ is technology-independent and the combination of references results in a product or process that is more desirable, for example because it is stronger, cheaper, cleaner, faster, lighter, smaller, more durable, or more efficient. Because the desire to enhance commercial opportunities by improving a product or process is universal-and even common-sensical-we have held that there exists in these situations a motivation to combine prior art references even absent any hint of suggestion in the references themselves. In such situations, the proper question is whether the ordinary artisan possesses knowledge and skills rendering him capable of combining the prior art references.” *Id.* 1368, 80 USPQ2d at 1651 (emphasis added).”

The Examiner has not overcome applicants’ traversal. The Supreme Court’s decisions control, not lower courts or the MPEP. The Examiner has not factually resolved in the record the level of ordinary skill in the art, so his above quotations are of no weight in this matter.

The Office Action stated that responding to applicants’ arguments that because the term “ordinary artisan” is meaningless, the citation of *Ex parte Kubin*, is not relevant the level of one ordinarily skilled in the art has not been determined, as required by Patent Office and the Supreme Court, applicants are invited to peruse MPRP 2143.03, Part II:

**"II. < SPECIFYING A PARTICULAR LEVEL OF SKILL IS NOT NECESSARY WHERE  
THE PRIOR ART ITSELF REFLECTS AN APPROPRIATE LEVEL**

If the only facts of record pertaining to the level of skill in the art are found within the prior art of record, the court has held that an invention may be held to have been obvious without a specific finding of a particular level of skill where the prior art itself reflects an appropriate level. *Chore-Time Equipment, Inc. v. Cumberland Corp.*, 713 F.2d 774, 218 USPQ 673 (Fed. Cir. 1983). See also *Okajima v. Bordeau*, 261 F. 3d 1350, 1355, 59 USPQ2d 1795, 1797 (Fed. Cir. 2001)."

The Examiner is invited to review the Forward to the MPEP (8<sup>th</sup> Ed., Rev. 5, for example) that states:

"The Manual does not have the force of law or the force of the rules in Title 37 of the Code of Federal Regulations."

The cited Federal Circuit cases require factual analysis of the prior art (not merely the rejection references) and such analysis must be in the record. The Examiner has not done either of these requirements. As the CAFC said, the prior art "reflects" the level of skill in the art – a reflection is not the same as the object that is the subject the reflection. For example, stand back from a mirror and one sees a reflection that is smaller than oneself – hence the reflection may or may not be the level of ordinary skill in the art as defined by the prior art. This is one of the reasons why analysis of the prior art is necessary and must be placed in the record. To not do so, as here, denies applicants the right to agree or oppose and rebut an Examiner's analysis.

The Office Action stated: that in the instant case, Omura et al., Hershberger et al. and Borghi et al. issued in 1978, 1987 and 1992, respectively; and that the dates of these documents, one of which is 30 years old, clearly establish that the ordinary artisan of the present day would be fully knowledgeable of antibiotic isolation procedures from a fermentate including extraction, concentration, filtration methods, etc. Applicants traverse this statement. The Examiner did not show in the record that he had analyzed the prior art of record (that is, all

of the patents, references, etc., of record), did not put his analysis and factual support for and against his position in the record, did not factually establish that the so-called reflection was the same as the level of ordinary skill in the art, etc. The Examiner did not even follow the CAFC cases. This obviousness rejection is still fatally defective.

The Office Action stated that, responding to applicant's argument that Omura et al. teaches away from water-miscible organic solvent, Omura et al. clearly states that the ordinary artisan can use a "suitable solvent" (col. 6, lines 55 to 57). The extraction method of Omura et al. is not pertinent to applicants' filtration method.

The Office Action stated that it is well within the skill of the ordinary artisan to select extraction solvents. What is within the skill of the ordinary artisan is meaningless under Section 103(a).

The Office Action stated that Hershberger et al. provides examples of such solvents that are suitable for antibiotic extraction from a broth. This statement is clearly in error because Hershberger et al. treat the broth with the filtration method, not the extraction method.

The Office Action stated that, regarding applicants' argument that the pH range taught by Hershberger et al. teaches away from using a pH of greater than 8.5 for staurosporine isolation, said limitation was taught by Omura et al. Since all of the prior art teachings of record must be considered, the Examiner has not factually shown or proven why the teaching of Hershberger et al. are to be ignored and that of Omura et al. chosen instead by one ordinarily skilled in the art.

The Office Action stated that, regarding applicants' argument that it is improper to make a multi-reference rejection for a multi-step process based on a single reference that teaches only one step, antibiotic isolation is an art having well known techniques. Omura et al. uses solvent extraction of the broth, which has nothing to do with applicants' filtration method. Omura et al. only mentions the filtration method.

The Office Action stated: that Omura et al. specifically teaches that staurosporine recovery can be achieved by “known methods for separating antibiotics” (col. 6, lines 41 and 42); and that, thus, the isolation of staurosporine by the claimed method is obvious in the absence of unexpected results. Unexpected results do not have to be shown by applicants because the Examiner has not even stated to whom the claimed method would be obvious.

Applicants’ claims have been limited tetrahydrofuran solvent – the amended claims are clearly unobvious to one ordinarily skilled in the art over the combination of rejection references.

The Office Action stated that regarding the references that were submitted with the response filed September 2, 2008, applicants are invited to specifically point out how each reference supports his/her position. Such references are part of the prior art of record which the Examiner must consider and analyze in his required factual resolution in the record of the level of ordinary skill in the art.

This rejection should be withdrawn.

Reconsideration, reexamination and allowance of the claims are requested



Respectfully submitted,

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